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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/802,674      | 03/09/2001  | Roberto A. Macina    | DEX-0142            | 9969             |

7590

04/07/2003

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EXAMINER

HARRIS, ALANA M

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 04/07/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Applicati n N .

09/802,674

Applicant(s)

MACINA ET AL.

Examiner

Alana M. Harris, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4. 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Response to Amendment and Arguments***

1. Claims 1-5 are pending.  
Claims 6 –10 have been cancelled.  
Claims 1-5 have been amended.  
Claims 1-5 are examined on the merits.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Information Disclosure Statement***

3. It was noted in the first action on the merits, Paper number 11 (mailed October 18, 2002) that the information disclosure statement filed July 16, 2001 as Paper number 4 cites references AD, AE, AQ, AR, AS and AU. Two of these references have been obtained and considered by the Examiner as denoted by the Examiners' initials listed beside references AR and AU (accompanying pages 2 and 3 of IDS filed July 16, 2001).

Applicants set forth that the remaining references are standard reference texts believed to be accessible to the United States Patent Office. And furthermore, Applicants aver that due to the voluminous nature of these texts copies are not being provided.

At this point in prosecution the documents that continue not to accompany the instant application for review are references AD, AE, AQ and AS. The Examiner

attempted to locate these references via interlibrary loan, however at the time of this office action they were not available.

The USPTO is obliged to accessing US Patents, as well as WO documents. However, any other documents considered relevant by Applicants should be submitted for consideration. The listed documents "lined through" were not reviewed during examination and not considered. In order to expedite prosecution it is requested that these references be supplied for consideration as set forth by 37 CRF § 1.98.

### ***Withdrawn Rejections***

#### ***Claim Rejections - 35 USC § 112***

4. The rejection of claims 1-5 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn in light of Applicants' arguments. Claim 7 has been cancelled.

5. The rejection of claims 1-5 set forth in Paper number 11 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn. Claim 7 has been cancelled.

***Claim Rejections - 35 USC § 101***

6. The rejection of claims 1-5 under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, credible or asserted utility or a well established utility is withdrawn in light of Applicants' arguments. Claim 7 has been cancelled.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 112***

7. Claims 2-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for diagnosing the presence of gastrointestinal cancer in a patient comprising determining levels of a polynucleotide comprising SEQ ID NO: 3 or a polynucleotide encoding a polypeptide comprising SEQ ID NO: 4 in cells, tissue or bodily fluids in a patient and comparing the determined levels of a polynucleotide comprising SEQ ID NO: 3 or a polynucleotide encoding a polypeptide comprising SEQ ID NO: 4 in cells, tissue or bodily fluids from a normal human control, wherein a change in determined levels of a polynucleotide comprising SEQ ID NO: 3 or a polynucleotide encoding a polypeptide comprising SEQ ID NO: 4 in said patient versus normal human control is associated with presence of gastrointestinal cancer, does not reasonably provide enablement for methods of diagnosing metastases, staging and monitoring changes in gastrointestinal cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicants' remarks received as Paper number 12 on page 11 verifies the nexus between Cln115 and SEQ ID NO: 3. The specification does set forth enabling disclosure supporting the occurrence of Cln115 underexpression in colon cancer interpreted as diagnostic of gastrointestinal cancer. This evidence is indicative of SEQ ID NO: 3 being a tumor marker for gastrointestinal cancer. However, the specification does not support the use of SEQ ID NO: 3 in methods of diagnosing metastases, staging and monitoring gastrointestinal cancer. There is no objective evidence in the specification that SEQ ID NO: 3, mRNA corresponding to SEQ ID NO: 3 or the protein (SEQ ID NO: 4) expressed from the polynucleotides would be useful as a marker of metastatic gastrointestinal cancer. It is well known in the art that metastatic cancer cells have altered patterns of gene expression in comparison with the non-metastatic precursor cancer cell. For instance, metastatic breast cancer cells are negative for E-cadherin expression, while normal breast cells and non-invasive breast cells are positive (Oka et al, Cancer Research, 1993, vol. 53, pp. 1696-1701). Uteroglobin is another example of a gene product, which is expressed in a primary tumor but not in metastatic cells released from said tumor (Weeraratna et al, Clinical Cancer Research, 1997, Vol. 3, pp. 2295-2300). These references demonstrate the lack of correlation between gene expression in a primary tumor versus metastatic cells released from said primary tumor. Therefore, it cannot be predicted that the polynucleotides effective in the diagnosis of gastrointestinal cancer would be expressed or effective in diagnosing metastatic gastrointestinal cancer and consequently useful in the monitoring and staging the said cancer. The specification does not provide sufficient guidance and

Art Unit: 1642

direction to implement SEQ ID NO: 3 and its corresponding protein in methods of diagnosing metastases, monitoring and staging gastrointestinal cancer.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The phrase "...hybridizes under stringent conditions..." in claims 1-5 is indefinite. The claims do not set forth the conditions encompassed by the phrase and necessary to implement the claimed invention. Accordingly, the metes and bounds of the claims cannot be determined. However, Applicants can obviate this rejection by amending the claims to recite the suggested claim language. For example, claim 1 could be amended to recite,

"A method for diagnosing the presence of gastrointestinal cancer in a patient comprising:

(a) determining levels of a polynucleotide comprising SEQ ID NO: 3 or a polynucleotide encoding a polypeptide comprising SEQ ID NO: 4 in cells, tissue or bodily fluids in a patient; and

(b) comparing the determined levels of a polynucleotide comprising SEQ ID NO: 3 or a polynucleotide encoding a polypeptide comprising SEQ ID NO: 4 in cells, tissue or bodily fluids from a normal human control, wherein a change in determined levels of a polynucleotide comprising SEQ ID NO: 3 or a polynucleotide encoding a polypeptide comprising SEQ ID NO: 4 in said patient versus normal human control is associated with presence of gastrointestinal cancer."



Art Unit: 1642

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

**ALANA HARRIS**  
**PATENT EXAMINER**  
*amharris*

Alana M. Harris, Ph.D.  
April 5, 2003